DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

TRANSMITTED BY FACSIMILE

Joanne Robinett
sanofi-aventis U.S. LLC
P.O. Box 5925
55 Corporate Drive
Bridgewater, NJ 08807

RE: NDA # 21-287
UROXATRAL® (alfuzosin HCl) Extended-Release Tablets for Oral use
MACMIS # 17961

Dear Ms. Robinett:

The Division of Drug Marketing, Advertising, and Communications (DDMAC) has reviewed a Voucher Tent Card (US.ALF.09.04.002) (tent card) for UROXATRAL® (alfuzosin HCl) Extended-Release Tablets (UROXATRAL) submitted by sanofi-aventis U.S. LLC (sanofi) under cover of Form FDA-2253. The tent card is misleading in that it presents efficacy claims for UROXATRAL, but fails to communicate its indication or information about the risks associated with its use. Thus, the tent card misbrands the drug in violation of the Federal Food, Drug, and Cosmetic Act (the Act), 21 U.S.C. 352(a) & 321(n). *Cf*. 21 CFR 202.1(e)(3)(i); (e)(5) & (e)(6)(i). In addition, it appears that the tent card was accompanied by an outdated version of the FDA-approved product labeling (PI) for UROXATRAL, in violation of 21 CFR 201.100(d).

Background

According to the Indications and Usage section of the PI:[1]

> UROXATRAL is indicated for the treatment of signs and symptoms of benign prostatic hyperplasia . . . .

UROXATRAL is associated with a number of important contraindications, warnings, and precautions. The PI for UROXATRAL contraindicates use in patients with moderate or severe hepatic impairment and co-administration with potent CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, ritonavir). The Warnings and Precautions section of the PI notes the occurrence of postural hypotension and Intraoperative Floppy Iris Syndrome (IFIS) and the need for caution in patients with renal or hepatic impairment. The Warnings and Precautions section also indicates that prostatic carcinoma should be ruled out prior to treatment with UROXATRAL. Furthermore, the adverse reactions associated with UROXATRAL include dizziness, upper respiratory infection, headache, and fatigue.

[1] The PI submitted with the promotional piece on Form FDA-2253 was dated August 2008. However, the tent card was submitted on June 30, 2009, with a listed dissemination date of June 30, 2009. The most current version of the FDA-approved PI for UROXATRAL at the time of dissemination is dated May 20, 2009 and is the version referred to in this letter.

Omission of Indication and Risk Information

Promotional materials are misleading if they fail to reveal facts that are material in light of the representations made by the materials or with respect to the consequences that may result from the use of the drug as recommended or suggested by the materials. The front side of the tent card presents effectiveness claims for UROXATRAL but fails to adequately communicate its indication or any risk information associated with its use.

The front side of the tent card contains the following statements: "**ALWAYS IN THE BATHROOM . . . especially at night?**" and "***Relief begins with U***" (emphasis in original). In the absence of the full indication, these statements misleadingly imply that UROXATRAL is approved for use in the treatment of any condition that keeps the patient in the bathroom, such as overactive bladder. However, UROXATRAL is only approved for use in the treatment of the signs and symptoms of benign prostatic hyperplasia (BPH). The omission of the indication on the front side of the tent card may encourage the use of UROXATRAL in circumstances other than those for which the drug has been shown to be safe and effective.

We note that the indication and risk information for UROXATRAL are printed on the back side of the tent card; however, the tent card is designed to be adhered to a flat surface (e.g., a pharmacy counter) and as a practical matter, viewers of the front side of the card are unlikely to be able to view the back side of the card once it is stuck in place. Presenting the indication and risk information in this manner is not sufficient to ensure that the claims in each part of the tent card are truthful and non-misleading. *Cf.* 21 CFR 202.1(e)(3)(i). Furthermore, your failure to include any risk information on the front side of the tent card cannot be corrected merely by including the statement "Please see Important Safety Information on back . . ." at the bottom of the front side of the tent card.

In addition to the complete omission of risk information from the front side of the tent card, the risk information that is included on the back side of the tent card under "Important Safety Information" fails to include an important warning and precaution regarding Intraoperative Floppy Iris Syndrome (IFIS). Specifically, the tent card fails to reveal that if patients are planning to have cataract surgery, they should tell their ophthalmologist that they are using UROXATRAL or have previously been treated with an alpha-blocker.

Use of Outdated Product Labeling

It appears that the tent card was disseminated with an outdated version of the PI, in violation of 21 CFR 201.100(d). The PI submitted with the promotional piece on Form FDA-2253 was dated August 2008. However, the listed dissemination date of the tent card was June 30, 2009; the most current version of the FDA-approved PI as of this date is the May 20, 2009 version, not the August 2008 version.

Conclusion and Requested Action

For the reasons discussed above, the tent card misbrands UROXATRAL in violation of the Act, 21 U.S.C. 352(a) & 321(n). *Cf*. 21 CFR 202.1(e)(3)(i); (e)(5) & (e)(6)(i). In addition, it

appears that the tent card was accompanied by an outdated version of the FDA-approved PI for UROXATRAL, in violation of 21 CFR 201.100(d).

DDMAC requests that sanofi immediately cease the dissemination of violative promotional materials for UROXATRAL such as those described above. Please submit a written response to this letter on or before November 6, 2009, stating whether you intend to comply with this request, listing all promotional materials (with the 2253 submission date) for UROXATRAL that contain violations such as those described above, and explaining your plan for discontinuing use of such violative materials.

Please direct your response to the undersigned at the Food and Drug Administration, Center for Drug Evaluation and Research, Division of Drug Marketing, Advertising, and Communications, 5901-B Ammendale Road, Beltsville, MD, facsimile at 301-847-8444. In all future correspondence regarding this matter, please refer to MACMIS # 17961 in addition to the NDA number. We remind you that only written communications are considered official.

The violations discussed in this letter do not necessarily constitute an exhaustive list. It is your responsibility to ensure that your promotional materials for UROXATRAL comply with each applicable requirement of the Act and FDA implementing regulations.

Sincerely,

{See appended electronic signature page}

Carrie Newcomer, PharmD
Regulatory Review Officer
Division of Drug Marketing,
Advertising, and Communications

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-21287	ORIG-1	SANOFI AVENTIS US LLC	UROXATRAL (ALFUZOSIN HCL)

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

CARRIE A NEWCOMER
10/23/2009